

Macroglossia in Acromegaly and Hypothyroidism

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Summary. The tongues of two patients with macroglossia were examined at autopsy. One of the patients had acromegaly and the other had hypothyroidism. To evaluate the size of the enlarged tongues, the average weight of the tongue in the human adult was determined first in a series of 20 unselected autopsies, 10 males and 10 females (ages 44 to 85). The weight of the tongue was greater in males than in females and was directly correlated with the height of the subject. Cachexia had relatively little effect on the weight. In acromegaly (case 21) and myxedema (case 22) the tongue was enlarged by at least 50%. Histopathology showed enlargement of muscle fibers especially anteriorly in acromegaly and hypothyroidism, thickening of the epithelium and increased subepithelial and interstitial connective tissue. Incidental findings included venous thrombi and telangiectasia in the subepithelial connective tissue in both hypothyroidism and acromegaly and a corpus amylaceum and two islands of hyaline cartilage in the tongue of hypothyroidism.

Key words: Tongue — Macroglossia — Acromegaly — Hypothyroidism.

Introduction

It is well known to clinicians and pathologists alike that the tongue is enlarged in a number of diseases (Cohen Jr., 1971; Dockerty et al., 1968; Lever, 1975; Rook et al., 1968; Sauk, 1970; Seifert, 1966; Seifert, 1974) including endocrine, metabolic and genetic disorders (Goodman and Gorlin, 1970) such as acromegaly (Ardran and Kemp, 1972; Rezek and Millard, 1963; Seifert, 1966; Seifert, 1974), hypothyroidism (Rezek and Millard, 1963; Seifert, 1966; Seifert, 1974), amyloidosis (Dockerty et al., 1968; Domonkos, 1971; Lever, 1975; Richter and Löblich, 1973; Seifert, 1966; Seifert, 1974), trisomy 21 (Ardran et al., 1972; Seifert, 1974), neurofibromatosis (Dockerty et al., 1968; Seifert, 1974), hyalinosis cutis et mucosae (lipoid proteinosis) (Domonkos, 1971; Seifert, 1966), erythro-

Table 1

Case No.	Age	Sex	Race	Diagnosis
1	47	F	N	Adenocarcinoma of uterus, carcinoma of urinary bladder
2	55	F	C	Carcinoma, breast, with metastases
3	85	F	C	Sarcoma of uterus
4	51	F	C	Malignant teratoma with metastases
5	61	F	C	Carcinoma, breast, with metastases
6	44	F	C	Perforated appendicitis and peritonitis, cirrhosis
7	52	F	N	Squamous cell carcinoma of lung with metastases
8	70	F	C	Diabetes mellitus, urinary infection, sepsis
9	45	F	C	Alcoholic liver disease, chronic pancreatitis
10	68	F	N	Gram negative sepsis, multiple abdominal fistulas
11	49	M	C	Cirrhosis
12	48	M	C	Huntington's chorea, cachexia
13	83	M	C	Carcinoma of prostate
14	50	M	C	Carcinoma of lung
15	65	M	N	Cerebral infarct, diabetes mellitus, bronchopneumonia
16	65	M	C	Ruptured esophageal varices, cirrhosis
17	72	M	C	Congestive heart failure
18	73	M	C	Bronchopneumonia, old cerebral infarct, cachexia
19	60	M	C	Adenocarcinoma of rectum, perforated colon, pelvic abscess
20	77	M	N	Bronchopneumonia, diabetes mellitus
21	63	F	C	Acromegaly, operated 1970
22	74	F	C	Hypothyroidism

blastosis fetalis and the Wiedemann-Beckwith syndrome (exomphalos-macroglossia-gigantism, or EMG syndrome) (Kirchner and Lee, 1975; Penchaszadeh, 1971). Macroglossia also occurs in glossitis granulomatosa associated with the Melkersson-Rosenthal-Syndrome (Seifert, 1966), and, it can be caused by vascular lesions, cysts, and benign and malignant tumors (Dockerty et al., 1968; Seifert, 1966; Seifert, 1974). Pure muscular macroglossia can be found in partial gigantism (Seifert, 1966) or it can present as congenital muscular hyperplasia without recognizable cause. However, the histopathology of the tongue in some of these disorders has been relatively neglected. This paper reports gross and microscopic findings in the tongue in a case of acromegaly and a case of hypothyroidism. To evaluate these findings, the normal tongue was investigated in a series of 20 unselected autopsies. The weight of the tongue and the relationship of weight to sex, height and weight of the body were determined. The histology of the normal tongue was compared to that of the enlarged tongue in acromegaly and hypothyroidism, respectively.

Materials and Methods

The weight of the tongue was determined in a woman of 63 with acromegaly, a woman of 74 with hypothyroidism, and in 20 unselected autopsies, 10 females and 10 males (Table 1). The

Tongue weight (g)	Body weight (kg)	Body length (cm)	Ratio tongue to body weight	Ratio tongue (g) to body length (cm)	Tongue as % of body weight	Dentition
95	104.3	155	0.0009	0.61	0.091	carious teeth
55	49.9	155	0.0011	0.35	0.110	few lower teeth
75	49.9	155	0.0015	0.48	0.150	edentulous
72	47.6	160	0.0015	0.45	0.15	edentulous
108	58.9	160	0.0018	0.68	0.183	normal
77	70.4	165	0.0010	0.47	0.109	Partially edentulous
70	56.9	165	0.0012	0.43	0.123	edentulous upper jaw
88	56.9	165	0.0015	0.53	0.155	edentulous
78	70.4	170	0.0011	0.458	0.111	edentulous
90	104.3	170	0.0009	0.529	0.086	normal
82	56.9	155	0.0014	0.53	0.144	edentulous
74	40.8	165	0.0018	0.45	0.181	carious teeth
110	56.9	165	0.0019	0.67	0.193	edentulous
90	58.9	170	0.0015	0.53	0.153	carious teeth
97	61.2	170	0.0016	0.57	0.158	normal
110	104.3	170	0.0011	0.65	0.105	few upper teeth
110	52.2	170	0.0021	0.65	0.210	few lower teeth
90	49.9	170	0.0018	0.53	0.180	edentulous
110	63.5	175	0.0017	0.63	0.173	normal
100	72.5	175	0.0014	0.57	0.138	edentulous
150	86.1	165	0.0017	0.91	0.174	edentulous/dentures
145	110.9	165	0.0013	0.88	0.131	edentulous

tongue was removed according to the method described by Baker (1967). The skin of the neck was reflected and the submental region undermined. An amputation knife was used to cut through the floor of the mouth, beginning at the midline and cutting posteriorly along the mandible on each side. The tip of the tongue then was pulled caudally, and the soft palate was separated from the hard palate. The dissection was continued posteriorly toward the spine, and the neck organs were removed by traction. Palatine tonsils, soft palate and hyoid bone were dissected from the tongue. Samples were taken from the base, the dorsolateral aspect posteriorly and anteriorly and the tip of the tongue. The sections were stained with hematoxylin-eosin, Pinkus' acid orcein-Giemsa, Verhoeff-Van Gieson, alcian blue pH 2.5 method with and without hyaluronidase digestion, PAS with and without digestion, Congo red and Sirius red. The thickness of the epithelium, subepithelial connective tissue and the muscle fibers at the root and the anterior dorsolateral aspect were measured with an ocular micrometer. The number of muscle fibers per low power field ($100\times$) was counted along a test line, according to the method of Weibel (1967). These measurements were tabulated and compared (Table 2). The Student's *t*-test was used to measure statistical significance. The special stains for connective tissue, mucopolysaccharides, glycogen and amyloid were evaluated and compared.

Results

In both sexes, the average weight of the tongue varied with the height of the individual. In women the tongue weighed less than in men, averaging 80.0 g (range 55–108 g). The tongue in men was about 20% heavier, averaging 97.3 g

Table 2. Microscopic tongue measurements

	Control 80 g		Acromegaly 150 g		Hypothyroidism 145 g	
	base	anterior	base	anterior	base	anterior
Diameter of muscle fibers	37 μ	18 μ	40 μ	36 μ	35 μ	38 μ
Thickness of epithelium	160 μ	160 μ	196 μ	810 μ	228 μ	147 μ
Thickness of subepithelial connective tissue	1630 μ	355 μ	1870 μ	843 μ	1475 μ	574 μ
Average number of muscle fibers/1 mm test line (Weibel and Elias 1967)	32	32	21	22	21	25

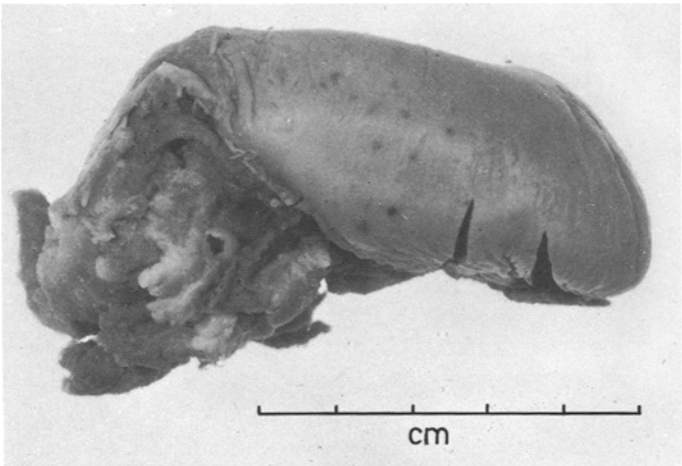


Fig. 1. Lateral aspect of tongue in female with hypothyroidism. Thickness 3.0 cm at different sites. Length 11.0 cm. Greatest width 6.6 cm

(range 74 – 110 g). True enlargement was found in the woman with acromegaly (case 21) whose tongue was large and weighed 150 g. (During life, occlusion of her dentures was noted to edge to edge in rest position.) In the woman with hypothyroidism (case 22) the tongue also was enlarged and weighed 145 g (Fig. 1). Thus, in each of these women the tongue was more than 50% greater than the average weight in men (97.3 g) and more than 80% greater than the average weight in women (80.0 g). The ratio of the tongue weight in grams to body length in centimeters averaged 0.58 in the males, 0.50 in the females and 0.90 in the two patients with enlarged tongues (case 21 and 22). However, when the weight of the tongue was related to the weight of the body, no consistent pattern was found. Furthermore, there was no reduction of the weight of the tongue in cachexia and emaciation (case 12 and 18).

Histologic studies of normal tongues revealed the following. The thickness of the epithelium averaged 160 μ throughout (Fig. 4). The subepithelial connec-

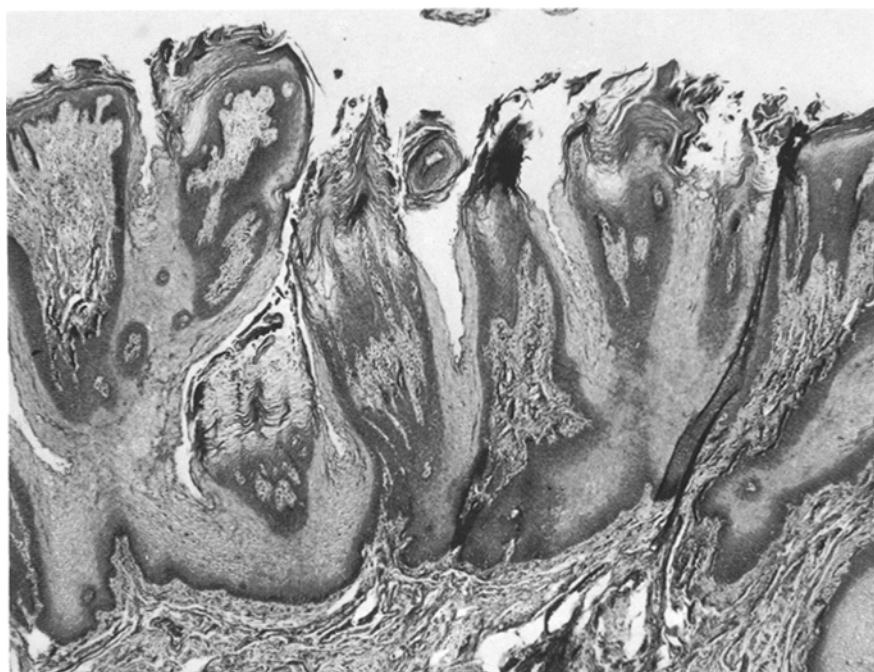


Fig. 2. Epithelium of dorsum of tongue, acromegaly (30 \times)

tive tissue measured 1630 μ at the base but only 355 μ in the anterior half. A few chronic inflammatory cells were present here. Elastic fibers were inconspicuous throughout. The muscle fibers averaged 37 μ in cross section at the base and 18 μ in the anterior half. The number of the muscle fibers per low power field (100 \times) averaged 32 both posteriorly and anteriorly. That is, in the normal tongues the diameter of the muscle fibers near the tip was only about one-half that of the fibers located posteriorly, though the number of fibers per low power field was the same.

In acromegaly, the epithelium was thickened due to marked acanthosis, and the filiform and fungiform papillae were unusually prominent (Fig. 2). The upper layer of the acanthotic epithelium contained PAS+ material resembling glycogen, which was not demonstrable after diastase digestion. Elastic fibers were unremarkable. In comparison with the control tongues, the muscle fibers were slightly enlarged posteriorly, and the diameter of the fibers in the anterior half was doubled. However, the number of muscle fibers per low power field (100 \times) was less than normal. The thickness of the subepithelial connective tissue was slightly increased throughout. These findings suggest that the enlargement of the tongue in acromegaly is due to thickening of the epithelium, and subepithelial connective tissue and enlargement of the muscle fibers in the anterior half of the tongue. The sections also disclosed increased amounts of connective tissue anteriorly, a small venous thrombus anteriorly and atrophic glands posteriorly.

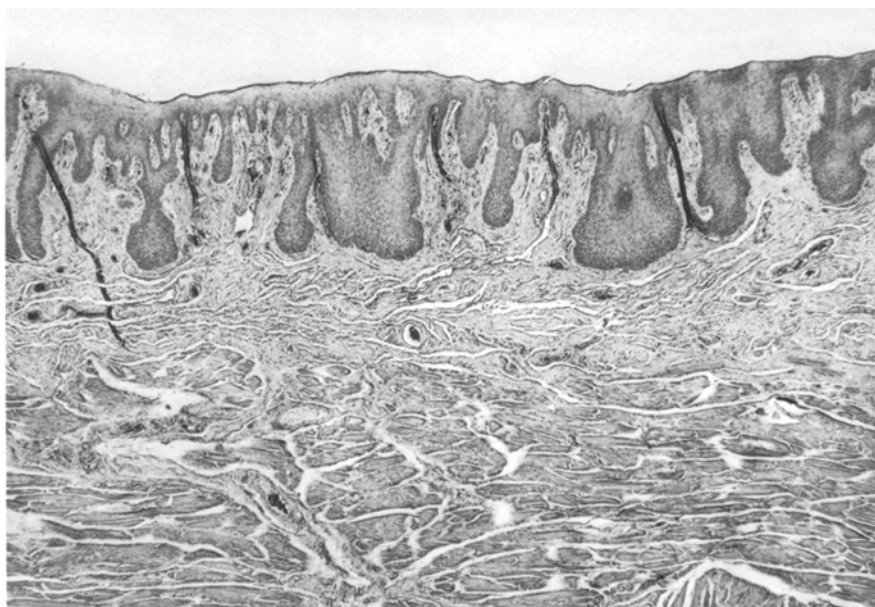


Fig. 3. Epithelium of dorsum of tongue, hypothyroidism (30 \times)

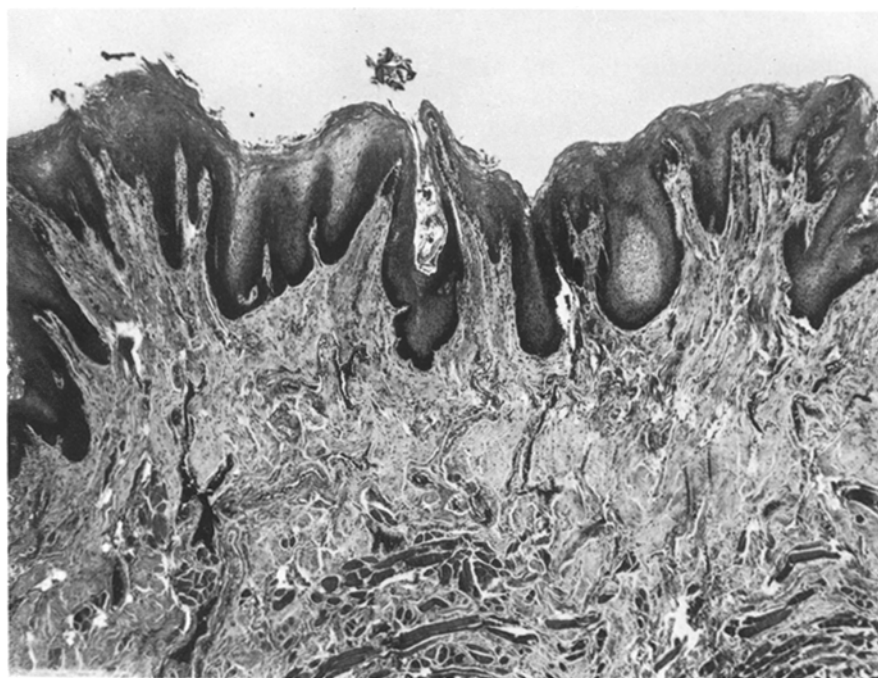


Fig. 4. Epithelium of dorsum of normal sized tongue (30 \times)

In hypothyroidism the epithelium was thickened posteriorly but was thinner than normal in the anterior half. In contrast to acromegaly, the tongue had a smooth appearance grossly, the surface of the epithelium was flat, and the papillae were not prominent (Fig. 3). The subepithelial connective tissue was thickened slightly in the anterior half but was thinned posteriorly. Elastic fibers were inconspicuous. The diameter of the muscle fibers was more than double the normal size in the anterior half but was not significantly changed posteriorly. The number of muscle fibers per low power field was less than normal throughout. Increased numbers of round cells were present in the subepithelial connective tissue, as well as focal telangiectasia and a few small venous thrombi of microscopic size. No basophilic degeneration of muscle fibers was encountered. A small corpus amylaceum and two small circumscribed foci of hyaline cartilage were present at the inferior aspect of the anterior half. The findings suggest that the enlargement of the tongue in hypothyroidism was caused by increase in diameter of muscle fibers in the anterior half.

Discussion

This study has demonstrated that the average weight of the human adult tongue is 90 g plus or minus 30 g. Body weight, dentition, cachexia and emaciation have no apparent effect on the weight of the tongue. Ardran and Kemp (1972) have speculated that the tongue may enlarge in partial edentia, but the findings in this study are not confirmatory. On the other hand, the weight of the tongue is closely correlated with the height of the subject. In general, the taller the individual, the heavier the tongue. The weight is quite different in the two sexes, being heavier in men. The thickness of the epithelium in the normal tongue is 160 μ throughout. The subepithelial connective tissue is thicker posteriorly measuring 1630 μ at the base but only 355 μ anteriorly. In the normal tongue, the diameter of the fibers anteriorly is smaller than those in the base; however, the numbers of fibers per high power field is the same throughout.

The study confirms that enlargement of the tongue is real in acromegaly and hypothyroidism, two endocrine disorders in which the tongue is enlarged clinically. The enlargement appears due in part to increased diameter of the muscle fibers, especially those in the anterior half. In acromegaly, thickening of the epithelium and subepithelial connective tissue contribute to the enlargement. The presence of the two islands of cartilage in the tongue of the woman with hypothyroidism is unexplained, and search of the literature has failed to reveal a similar case. In any event, it seems unlikely that these microscopic foci made a significant contribution to the increased weight of the tongue.

The muscle fibers of the tongue might be expected to exhibit basophilic degeneration in myxedema, resembling the change characteristically seen in muscle fibers of the heart (Doerr, 1970). Doerr has observed a similar pattern of reaction in muscle fibers of the tongue in hypothyroidism (Doerr, personal communication). However such changes were not found in the case reported here.

Acknowledgment. I thank Professor Nancy E. Warner, Chairman, Department of Pathology, University of Southern California for helpful advice in preparation of this paper.

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Received October 4, 1976